

SPECIFICATION

This application is a JNK INHIBITORS
Technical Field *371 of PCT/JP03/15481 filed on 12/03/2003.*

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Entered
9/10/07*

The present invention relates to JNK inhibitors which are useful for treatment of a brain neurodegenerative disorder or the like. The present invention also relates to indazole derivatives or pharmaceutically acceptable salts thereof which have JNK inhibitory activity and are useful for treatment of a brain neurodegenerative disorder or the like.

Background Art

JNK (c-Jun N-terminal kinase) is an enzyme which is activated by physical or chemical stresses such as hypertonic stimulation, ultraviolet rays or a protein synthesis inhibitor, or cytokine such as TNF- α (tumor necrosis factor- α) or IL-1 (interleukin-1) and which phosphorylates Jun which is an AP-1 (activator protein-1) transcription factor to increase its transcription activity; and it is related to stress response and apoptosis. In particular, it is known that JNK plays an essential role in apoptosis of PC12 cells caused by removal of serum and in apoptosis mediated by ceramide and that JNK is activated during apoptosis of various cell strains and primary culture of striatum nerve cells of newborn rats [Nippon Rinsho, volume 56, page 1779 (1998); Journal of Biological Chemistry, volume 273, page 3756 (1998)].

It has been known at present that there are three subtypes